



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>7</sup> : C12Q 1/68	A1	(11) International Publication Number: WO 00/36142
		(43) International Publication Date: 22 June 2000 (22.06.00)

(21) International Application Number: PCT/CA99/01177

(22) International Filing Date: 10 December 1999 (10.12.99)

(30) Priority Data:  
60/111,794 11 December 1998 (11.12.98) US

(71) Applicant (for all designated States except US): VISIBLE GENETICS INC. [CA/CA]; 700 Bay Street, P.O. Box 333, Toronto, Ontario M5G 1Z6 (CA).

(72) Inventor; and

(75) Inventor/Applicant (for US only): SHIPMAN, Robert [CA/CA]; #2-6240 Montevideo Road, Mississauga, Ontario L5N 2N7 (CA).

(74) Agent: DEETH WILLIAMS WALL; National Bank Building, Suite 400, 150 York Street, Toronto, Ontario M5H 3S5 (CA).

(81) Designated States: AU, CA, JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

## Published

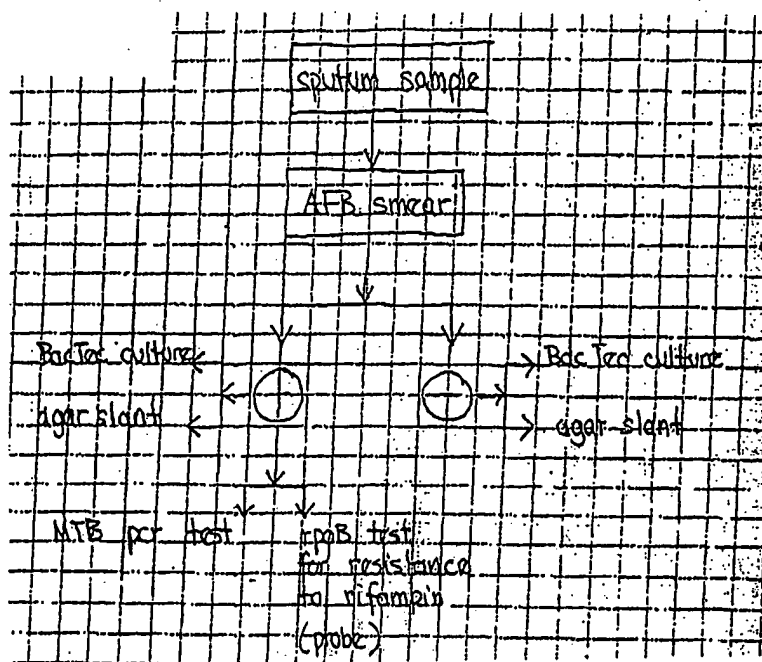
With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: METHOD AND KIT FOR THE CHARACTERIZATION OF ANTIBIOTIC-RESISTANCE MUTATIONS IN *MYCOBACTERIUM TUBERCULOSIS*

## (57) Abstract

Amplification and cycle sequencing primer sets have been developed for the detection and analysis of antibiotic resistance-associated mutations in defined regions of the *rpoB* (rifampin), *katG* (isoniazid), *oxyR-ahpC* PR (isoniazid), *mabA* (isoniazid), *rpsL/s12* (streptomycin), *16S/rrs* (streptomycin), *embB* (ethambutol), *pncA* (pyrazinamide), *gyrA* (ciprofloxacin) and *23S* (azithromycin) genes of *Mycobacterium tuberculosis*. These primers can be used in a method for detection and characterization of *Mycobacterium tuberculosis* present in a sample. The method includes the steps of obtaining a sputum sample suspected of containing *M. tuberculosis*, performing a first sequencing procedure, with or without prior amplification, on the sample to detect the presence of *M. tuberculosis*, and if present to evaluate the *rpoB*, *katG*, *rpsL/s12* and *23S* genes for the presence of antibiotic-resistance inducing mutations; and (c) if *M. tuberculosis* is detected in step (b), performing a second sequencing procedure, with or without prior amplification, on the sample to evaluate the additional genes for the presence of antibiotic-resistance inducing mutations.



**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						